Contrast enhanced imaging of human meniscus using cone beam CT


Introduction

The crescent shaped menisci, locating between the medial and lateral condyles of femur and the tibial plateau, bear and distribute loads within the knee, stabilize the knee joint, absorb shocks and improve joint lubrication.1,2 The menisci are fibrocartilaginous tissue, principally composed of water (60–75%), collagens (mainly type I) (15–25%) and proteoglycans (PGs) (1–2%).3,5 Meniscal injuries or degeneration reduce the shock-absorbing capabilities of the menisci, and can lead to mechanical overloading of articular cartilage and eventually to knee osteoarthritis (OA)6,7. Hence, prompt detection of meniscal pathologies is important for the successful treatment and prevention of OA.

The diagnosis of meniscal damage is currently mainly based on magnetic resonance imaging (MRI) and to a lesser degree on computed tomography (CT) arthrography8–10. It has been postulated that contrast enhanced CT (CECT) imaging, an equivalent X-ray technique to delayed gadolinium enhanced MR-imaging of cartilage (dGEMRIC), could be exploited in the detection of cartilage injuries and degeneration11–14. Although CT imaging delivers ionizing radiation, the new generation cone beam scanners provide lower doses15 with higher image resolution. CECT has also been shown to detect a decrease in cartilage PG content16,17.

Recently, the CECT technique was successfully applied with bovine meniscus in vitro18. Since PGs contain negatively charged glycosaminoglycans (GAGs), the anionic contrast agent (CA) often applied in CECT is assumed to distribute mainly by diffusion into the tissue and to equilibrate in inverse proportion to the spatial distribution of GAGs. However, based on the present results, shorter delay between injection and imaging (e.g., 40 min) could be feasible in clinical diagnostics of meniscal pathologies.

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**SUMMARY**

Objective: Meniscal injuries can lead to mechanical overloading of articular cartilage and eventually to knee osteoarthritis. The objective was to evaluate the potential of contrast enhanced computed tomography (CECT) to image contrast agent (CA) diffusion in human meniscus with a clinical cone beam CT scanner.

Design: Isolated human menisci (n = 26) were imaged using magnetic resonance imaging (MRI) and CECT in situ. Diffusion of anionic CA into the meniscus was imaged for up to 30 h. The results of CECT were compared with water, collagen and proteoglycan (PG) contents, biomechanical properties, age and histological and MR images of the samples.

Results: Diffusion of CA required over 25 h to reach equilibrium. The CA partition (the CA concentration in the tissue divided by that in the bath) at the 40 min time point correlated significantly with that at the 30 h time point in both lateral (r = 0.706, P = 0.007) and medial (r = 0.669, P = 0.012) menisci. Furthermore, CA partition in meniscus after 30 h of diffusion agreed qualitatively with the distribution of PGs.

Conclusion: The cross-sectional distribution of CA was consistent with that reported in a previous μCT study on bovine meniscus. The time required to reach diffusion equilibrium was found impractical for clinical applications. However, based on the present results, shorter delay between injection and imaging (e.g., 40 min) could be feasible in clinical diagnostics of meniscal pathologies.

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distribution of PGs. Similar to articular cartilage degeneration, PG depletion is one of the first signs of meniscal degeneration. However, alike in articular cartilage, CA diffusion and distribution may be influenced also or even more by other factors in the meniscus, e.g., collagen and water contents as well as the presence of micro cracking of the matrix.

The present study is the first to evaluate the potential of CECT for imaging CA diffusion in isolated human menisci by using a clinical peripheral cone beam CT (CBCT) scanner. The aim of this study was to assess whether CECT could be used to detect spontaneous degeneration or injury of the meniscus, by comparing CECT findings with quantitative histological, compositional and biomechanical properties of the meniscus.

Materials and methods

Sample preparation

A total of 26 menisci were acquired from the left knee joints of human cadavers (n = 13, mean age 53.5 years, ranging from 24 to 76, 12 male, 1 female) with no history of joint disease (National Agency of Medicolegal Affairs, Helsinki, Finland; permission 1781/32/200/01). The menisci were stored at −25 °C until the experiment.

Magnetic resonance imaging

The experiment started with MR imaging. The menisci, while immersed in phosphate buffered saline (PBS), were imaged utilizing a standard clinical MRI-protocol for the knee joint. To prevent the degradation of the menisci, penicillin-streptomycin (100 units ml⁻¹ penicillin, 100 μg ml⁻¹ streptomycin; EuroClone, Siziano, Italy), antmycotic agent (Gibco Fungizone Antimycotic, 250 μg ml⁻¹ amphotericin B, 205 μg ml⁻¹ sodium deoxycholate; Life Technologies, Carlsbad, CA, USA) and inhibitors of proteolytic enzymes [5 mM ethylenediaminetetraacetic acid disodium salt (EDTA); VWR International, Fontenay, France] and 5 mM benzamidine hydrochloride hydrate (Sigma–Aldrich Inc., St. Louis, MO, USA) were added to PBS. For imaging, a clinical 3.0 T magnet (Achieva-3T, Philips Medical Systems, Amsterdam, Netherlands) was used with seven different imaging sequences: four T2-weighted spectral attenuated inversion recovery (SPAIR) sequences (three acquisitions in the sagittal plane, TR = 4150 ms, TE = 52 ms, in-plane resolution = 0.36 mm, slice thickness = 1.5, 2.0 and 3.0 mm; one acquisition in the coronal plane, TR = 4150 ms, TE = 52 ms, in-plane resolution = 0.36 mm, slice thickness = 2.0 mm), T1-weighted adiabatic turbo spin-echo (aTSE) sequence (sagittal plane, TR 581 ms, TE 20 ms, in-plane resolution 0.31 mm and slice thickness 2.0 mm), a sensitivity encoded (SENSE) proton density (PD) weighted TSE sequence (sagittal plane, TR 1800 ms, TE 40 ms, in-plane resolution 0.36 mm and slice thickness 2.00 mm) and a three-dimensional PD weighted SPAIR sequence (TR 13000 ms, TE 40 ms, in-plane resolution 0.28 mm and slice thickness 0.50 mm).

The blind coded images were interpreted and graded twice with at least 1 week interval by two experienced musculoskeletal radiologist. Based on this data, the intra- and intra-reader reliabilities were calculated. The menisci were graded according to Lotysz et al. and Crues et al.. Grade 0 is normal, grade 1 shows an intrameniscal globular signal that does not communicate with the articulating surfaces of the meniscus, grade 2 shows an intrameniscal linear or wedge-shaped signal not communicating with the articulating surfaces, and grade 3 shows an intrameniscal signal that communicates with at least one of the articulating surfaces. Furthermore, the signal increase was examined from all of the MRI slices in each meniscal region (anterior, central and posterior).

CECT imaging

The diffusion of anionic (q = −1) CA (Hexabrix, Mallinckrodt Inc., St. Louis, MO, USA) into the meniscus was studied using a modern clinical peripheral CBCT scanner (Verity, Planmed Oy, Helsinki, Finland). The diffusion of CA into the meniscus was imaged at 16 different time points for up to 30 h. Between the imaging sessions, the menisci were immersed in an isotonic bath (800 ml) of PBS (including penicillin-streptomycin, an antmycotic agent and proteolytic inhibitors) containing CA. In order to provide the best possible contrast in the image, the CA concentration was chosen to be 48 mg/ml. The bath was constantly agitated with a magnetic stirrer (C-Mag HS 7, IKA-Werke, Staufen, Germany) while kept at room temperature (20 °C). CBCT images were acquired with isotropic voxel size of 200 × 200 × 200 μm³ and 96 kV tube voltage. The tube voltage of 96 kV was chosen to provide optimal image quality with the used CA. After 30 h of immersion, the CA was washed out by immersing the menisci in PBS for 24 h. Subsequently, the menisci were wrapped in PBS dampened gauze and frozen until the biomechanical measurements, after which the menisci were cut into smaller sections for histological and compositional analysis.

CT data was analyzed using Analyze software (v. 10.0, AnalyzeDirect, Inc., KS, USA) and MATLAB (R2011a, MathWorks, Inc., Natick, MA, USA). The images were segmented using a semi-automatic threshold based algorithm and the meniscal tissue was isolated for further analysis. Subsequently, the meniscus was divided into three regions of interest (ROIs): anterior, central and posterior; each region being one third of the total length of the meniscus [Fig. 1(A)]. At every time point, the mean X-ray attenuation for each ROI was obtained by averaging the Hounsfield unit (HU) values over all pixels within the ROI. The mean partition of the CA, i.e., the CA concentration in the meniscus divided by that in the bath, was determined by subtracting the non-contrast images from those with the CA and normalizing with the mean HU value of the CA bath. The time for the diffusion to reach equilibrium within different ROIs was determined as the time at which the change in the CA partition was less than 0.1% per hour. Furthermore, three CECT cross-sectional slices were obtained from the same locations as the histological sections [Fig. 1(B)] and the mean X-ray attenuation of those slices was calculated. To investigate the cross-sectional CA distribution, the CECT slices were divided into inner, middle and outer subregions, with each subregion being one third of the total cross-sectional length [Fig. 1(C)].

Biomechanical measurements

First, the thickness of the meniscus tissue at the measurement site was measured with a digital caliper along the direction of indentation. Thereafter, the whole meniscus tissue was glued to the bottom of the measuring chamber which was then filled with PBS. The chamber was tilted such that the contact surface of the tissue was perpendicular to a cylindrical flat-ended steel indenter (Ø = 1.19 mm). The test was conducted by using a custom made material testing system including a high precision load cell (Model 31/AL311AR, Honeywell, Columbus, OH, USA; resolution: 0.005 N) and an actuator (PM1A1798, Newport Corporation, Irvine, CA, USA; resolution: 0.1 μm). Four compressive steps (4 × 5% of meniscus thickness) were applied using a ramp rate of 100%/s and a relaxation criterion of <10 Pa/min. The measurements were conducted for each meniscal region [Fig. 1(B)]. The equilibrium (the stress–strain–load (linear fit) from step 2 to 4) and instantaneous (step 4) moduli were calculated with Poisson’s ratios of μ = 0.1 and μ = 0.5, respectively, along Hayes et al.
Histology and compositional analyses

After the biomechanical measurements, the menisci were cut for histological and compositional analyses [Fig. 1(B)]. For the histological analysis, the samples were fixed in 10% formalin, processed in graded alcohol solutions, embedded in paraffin and cut into 3 μm thick sections; three per each region. These sections were stained with Safranin-O, which as a cationic dye, binds to negatively charged GAGs indicating the PG distribution within the meniscus. The spatial PG distribution of the stained sections was observed utilizing a light microscope (AxioImager M2, Carl Zeiss, Oberkochen, Germany). Furthermore, the spatial PG distribution of the stained sections was measured utilizing quantitative digital densitometry (DD) Measurement system consisted of a light microscope (Leitz Wetzlar, Wetzlar, Germany) using monochromatic light (λ = 492 ± 5 nm) and a pelting-cooled 12-bit CCD camera (CH250, Photometrics, Tucson, AZ, USA). Calibration of the system was done with neutral density filters (Schott, Mainz, Germany) covering optical density (OD) range from 0 to 3 OD.

For compositional analyses, one section (thickness = 1 mm) per each region was cut. From these sections, the water content was determined with the freeze drying method. Subsequently, hydroxyproline and uronic acid contents, which correspond to the collagen and PG contents respectively, were determined. To achieve this, the sections were incubated with a 1 mg/ml concentration of papain in 150 mM sodium acetate including 50 mM Cys-HCl and 5 mM EDTA at pH of 6.5 and 60 ºC for 3 h in order to digest the PGs. In order to inactivate the enzyme, the sections were boiled for 10 min. The hydroxyproline content was determined from the ethanol-precipitated sections. For each section, the hydroxyproline and uronic acid contents were determined three times and averaged. Furthermore, the contents were normalized to the wet weights of the sections to compensate for the variation in the section size.

Statistical analyses

Wilcoxon signed rank test was applied to study the significance of the differences between the parameter values determined for different meniscal locations and subregions (n = 13 for each location/subregion). For independent observations (n = 13 for each location), Pearson’s correlation coefficients (r) between the compositional, histological, biomechanical, MRI and CECT parameters were determined. Furthermore, multiple linear regression analysis was conducted between the compositional and biomechanical parameters and also between the compositional, MRI and CECT parameters. When comparing the other parameters with MRI grades, the median of all grading rounds was used. In case the median was a non-integer, the value was rounded up. To estimate the inter-reader reliability of MRI grading, the Cohen’s kappa coefficient (κ) was determined. When determining the kappa coefficient, the higher MRI grade of two rounds for each radiologist was used. In addition, the intra-reader reliabilities were calculated. The statistical tests were conducted using SPSS (v. 19.0.0.2, SPSS Inc., IBM Company, Armonk, NY, USA).

Results

In most samples, CA diffusion reached equilibrium after 25 h (Figs. 2 and 3). After 30 h of diffusion, the CA partition was significantly higher (P < 0.0001) in the lateral meniscus than in the medial meniscus. At this time point, the mean CA partition in the menisci varied from 53% to 78%. Furthermore, the mean CA partition was highest in the posterior horn and lowest in the central region in both medial and lateral menisci (Fig. 2, Table I).

The CA partition at the 40 min time point correlated significantly with that at 30 h time point in both lateral (r = 0.706, P = 0.007) and medial (r = 0.669, P = 0.012) menisci (Table II). In addition, in the lateral meniscus CA partition correlated significantly with the hydroxyproline content (r = −0.835, P = 0.0003) and age (r = −0.617, P = 0.025) at the 40 min time point, and with hydroxyproline content (r = −0.578, P = 0.039) and age (r = −0.649, P = 0.016) at the 30 h time point (Table II). There was no significant correlation between the MRI grading (for detailed MRI findings see Table III) and CA partition at the 30 h time point in either the medial meniscus (P = 0.841) or in the lateral meniscus (P = 0.970). The compositional constituents (water, hydroxyproline and uronic acid) and structure (MRI grade) were significantly related to the CA partition in lateral anterior horn (r = 0.888, F = 7.489, P = 0.008), posterior horn (r = 0.900, F = 8.563, P = 0.005) and in the whole meniscus (r = 0.857, F = 5.524, P = 0.020) after 40 min of diffusion. Furthermore, the compositional constituents and structure were significantly related to the CA partition in medial central region (r = 0.843, F = 4.914, P = 0.027) after 30 h of diffusion. The compositional constituents did not significantly relate to the biomechanical properties in either the medial meniscus (r = 0.835 and P = 0.297 for the instantaneous and equilibrium moduli, respectively) or the lateral meniscus (P = 0.486 and P = 0.393 for the instantaneous and equilibrium moduli, respectively).
The intra-reader reliabilities of the MRI grading were 65% and 82% for radiologist #1 and #2, respectively. The agreement between the radiologists was poor ($k = 0.126$, $P = 0.009$).

No significant correlations were found between the CA partition and PG content on either medial ($P = 0.684$) or lateral ($P = 0.128$) side. However, when the comparison included all of the menisci ($n = 26$), a modest negative correlation ($r = -0.390, P = 0.049$) was detected between the X-ray attenuation and PG content. Furthermore, the CA distribution in the meniscus after 30 h of diffusion showed inverse spatial agreement with the PG distribution.

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quantified by means of Safranin-O staining (Fig. 4), i.e., areas with most of the CA exhibited the smallest amount of PGs. The CA partition was highest in the outer cross-sectional subregion while the PG content was highest in the middle subregion (Fig. 5).

### Discussion

We investigated the potential of CECT to image anionic CA diffusion in the human meniscus in situ utilizing clinical peripheral
The CA partition varied significantly between different anatomical locations. Since the diffusion of CA into the different regions of the meniscus is poorly understood and the age and condition of the meniscus varied substantially, it is challenging to determine whether it was the patient-specific characteristics or the location-dependent properties which had the greatest effect on CA.

Table III

<table>
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<th>MRI grade</th>
<th>Radiologist #1</th>
<th>Radiologist #2</th>
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<tr>
<td></td>
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<td>0   1  2  3</td>
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<tr>
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<td>0   3  0  10</td>
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<td>central</td>
<td>3   1  7  2</td>
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<td>posterior</td>
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<td>0   10 0  3</td>
</tr>
<tr>
<td>Lateral meniscus</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>0   11 0  2</td>
</tr>
<tr>
<td>central</td>
<td>6   0  3  4</td>
<td>1   2  7  3</td>
</tr>
<tr>
<td>posterior</td>
<td>7   2  0  4</td>
<td>0   7  3  5</td>
</tr>
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</table>

Grade 0 is normal; Grade 1 shows an intrameniscal globular signal that does not communicate with the articulating surfaces of the meniscus; Grade 2 shows an intrameniscal linear or wedge-shaped signal not communicating with the articulating surfaces; Grade 3 shows an intrameniscal signal that communicates with at least one of the articulating surfaces.

from the differences in diffusion distance (tissue thickness) and the lower permeability of the meniscus. The diffusion proceeded approximately at the same speed through both articulating surfaces. Furthermore, the propagation of the CA was qualitatively similar in all anatomical locations. However, it must be noted that presently the diffusion through the periphery of the meniscus was not prevented, which is likely to allow reaching diffusion equilibrium sooner than in the clinical situation where diffusion mainly occurs through the articulating surfaces of the meniscus.

The time required to reach diffusion equilibrium in human meniscus (>25 h) is not practical for clinical application. However, as shown with cartilage in vivo, a shorter delay (e.g., 40 min) between injection and imaging could also be feasible in the diagnostics of meniscal pathologies. Meniscal tears and macroscopic lesions could be detected in arthrographic images acquired immediately after the administration of CAs, whereas detection of degeneration of internal structures could be interpreted from delayed images. This claim is supported by the positive correlation between the CA partitions after 40 min and 30 h of diffusion in both menisci (lateral: $r = 0.706, P = 0.007$; medial: $r = 0.669, P = 0.012$). Even though 40 min might not be sufficient to allow the CAs to diffuse completely through the meniscus, it could still indicate changes in the superficial tissue integrity. The possible increase in permeability due to degeneration or injury allows increased CA intake, and thus changes in the meniscus integrity could be detected in the delayed (40 min) image. Impaired integrity may also increase the CA partition at equilibrium, and thus enable correlation between these two time points. This is supported by earlier in vitro cartilage studies reporting good sensitivity of early time points in the detection of acute injuries and the strong correlation between early time points and diffusion equilibrium.

The CA partition varied significantly between different anatomical locations. Since the diffusion of CA into the different regions of the meniscus is poorly understood and the age and condition of the meniscus varied substantially, it is challenging to determine whether it was the patient-specific characteristics or the location-dependent properties which had the greatest effect on CA.
partition in different locations. Thus, in future studies, we propose that a comprehensive comparison of the diffusion properties in different meniscal regions should be carried out with fully intact and similarly aged menisci in vitro.

The CA partition in the meniscus after 30 h of diffusion showed qualitative inverse agreement with the spatial distribution of the PG content, as determined by means of light microscopy. This is consistent with a previous μCT study on bovine meniscus 18, reporting a moderate negative correlation ($R^2 = 0.51, P = 0.03$) between the X-ray attenuation and the GAG content at different meniscal regions. However, presently, no significant correlation was found between CA partition and the uronic acid content. Furthermore, a modest significant correlation between X-ray attenuation and OD values was only found when no subdivision into medial and lateral groups was performed. Even though the GAG content has been shown to correlate with the partitioning of anionic CA18, PGs do not exclusively govern the CA distribution34. This is supported by our finding that the PG content was significantly higher in the middle than in the inner or outer cross-sectional subregion, while the CA distribution increased significantly towards the outer subregion. In other words, we believe that no significant correlation between the CA partition and the uronic acid content or OD values were found due to the small amount of PGs in the meniscus34. Thus, the CA distribution in the meniscus is also affected by other factors, such as the tissue’s water and collagen contents, and the stercial hindrance created by the meniscus matrix.

As the CA bath was constantly agitated with a magnetic stirrer while the menisci were immersed, the CA solution was homogenous throughout the experiment. Thus, if any kind of increased intake of the CA occurred, this was probably due to the elevated osmotic environment is known to significantly affect the mechanical properties of cartilage46,47. However, in this study, isotonic solutions were always used. Thus, any possible CA residue in the meniscus did most likely not affect the biomechanical measurements.

MRI was conducted using multiple sequences used in standard clinical imaging of the knee joint. In the present study only native MRI sequences were used, although dGEMRIC is used in the evaluation of meniscal injuries35. Since it takes approximately as long for gadolinium to reach diffusion equilibrium as ioxaglate48, including dGEMRIC, in the present study the menisci should have been immersed in different solutions for an additional 54 h (30 and 24 h for diffusion-in and wash out, respectively). This might have jeopardized the integrity of the menisci. To avoid this, dGEMRIC of meniscus was not included in the study protocol.

The overall water and hydroxyproline contents were consistent with those previously reported for human and ovine menisci, respectively5,37. The equilibrium and instantaneous modulus values were consistent with those reported in most of the previous studies38,39. However, Moyer et al.40 reported significantly higher equilibrium and instantaneous moduli values. In their study, biomechanical properties were measured from the deep zone of the meniscus using a creep relaxation test with a significantly smaller indenter than applied in the present study (0.30 mm and 1.19 mm, respectively). It has been shown that the value of elastic modulus of cartilage is significantly dependent on the indenter size41. Even though the meniscus is not uniform in width, the meniscus width was always over 4 times the indenter diameter. Thus, the shape of the meniscus should not have exerted any significant effect on the results46,42.

Even though the patients had no history of joint diseases, slight degeneration, possibly due to relatively high average age (53.5 years) of the patients, was observed with MRI in more than a half of the menisci. Due to this factor and the relatively small number of joints ($n = 13$), the assessment of natural regional variation in compositional and biomechanical results is challenging and needs to be taken into account when interpreting the results. However, this was not the focus of the present study and thus does not jeopardize the conclusions. Present menisci went through two freeze–thaw cycles before CECT, which might have had a minor effect on the presented results43–45. In addition, the CA probably did not wash out completely during the 24 h PBS immersion46. The difference in the osmotic environment is known to significantly affect the mechanical properties of cartilage46,47. However, in this study, isotonc solutions were always used. Thus, any possible CA residue in the meniscus did most likely not affect the biomechanical measurements.

The low inter-rater agreement between the MRI grades suggests that the grading is a subjective and semi-quantitative method, even in the present optimal setup with isolated menisci. However, it must be noted that meniscus MRI grading is usually conducted using coarser grading systems that emphasize grading of different types of tears rather than assessing the intrameniscal signals, as done in the present study46,49.

Slight meniscal degeneration or intra-substance tears might not associate with aberrant loading of articular cartilage or mechanical knee instability. However, these types of meniscal injuries might eventually develop into full thickness tears introducing abnormal loading of the knee joint and cartilage. Thus, diagnosing the early stage changes of the meniscus would be important in the prevention of OA.

![Fig. 5.](image_url)
The correlations between CA partition, biomechanical and compositional properties were found to be more significant at 40 min of diffusion than at equilibrium. This is probably due to the varying properties (age and structural integrity) of the menisci which affect also their biomechanical and compositional properties. Furthermore, as 40 min and 30 h time points indicate different properties of the tissue (structural integrity and PG distribution, respectively), correlation between the CA partition and the tissue composition and biomechanical properties may be secondary at 40 min. In addition, the indentation testing tends to measure mostly the superficial characteristics rather than bulk properties of the tissue and the CA partition is more sensitive to the surface properties at early time points. We believe that for this reason the biomechanical parameters correlated more significantly with the CA partition at 40 min than at 30 h.

Indentation is not a commonly used method in evaluation of the meniscus due the shape of the tissue. However, indentation method was implemented in the present study as we wished to keep the samples intact and not extract tissue explants, e.g., for confined or unconfined compression tests. We also originally thought that indentation on fully intact meniscus would be the best measurement geometry to actually show the mechanical effect of internal degeneration/tears. Furthermore, we believe that this extraction could possibly have altered the biomechanical properties of the meniscus. Furthermore, based on our preliminary tests, the preparation of cylindrical plugs was extremely challenging and would have most likely produced artifacts.

Based on the present results, the delayed image (e.g., 40 min after CA administration) could possibly be utilized to evaluate the diffusion properties of the meniscus and therefore the integrity of the tissue. However, the clinical performance of the technique in the evaluation of integrity of the meniscus is not yet fully revealed. Thus, comprehensive in vitro and in vivo studies are still required. Furthermore, it must be noted that, to the authors’ best knowledge, this is the second CECT study of the meniscus, and the first study conducted with a clinical CBCT scanner and involving human meniscus. In order to better estimate the potential of CECT, as compared with MRI, in the clinical diagnostics of meniscal injuries, the comparison of MR and CECT image grading should be conducted. Furthermore, reproducibility of the grading of delayed and equilibrium CECT images should be compared with that of MRI grading.

In conclusion, the present results indicate the diagnostic potential of CECT of human meniscus using modern clinical peripheral CBCT scanner. However, further systematic studies will be needed to reveal the clinical potential of CECT.

**Contributions**

JTJH: The conception and design of the study, acquisition, analysis and interpretation of data, drafting the article, critical revision of the article for important intellectual content, final approval of the article.

EKD: The design, acquisition, analysis and interpretation of biomechanical data, critical revision of the article for important intellectual content, final approval of the article.

J-SS: Analysis and interpretation of MRI data, critical revision of the article for important intellectual content, final approval of the article.

VT: Acquisition and analysis of histological and compositional data, critical revision of the article for important intellectual content, final approval of the article.

RKK: The design and analysis of the biomechanical measurements, the design of histological samples, interpretation of data, obtaining funding, critical revision of the article for important intellectual content, final approval of the article.

JSJ: The conception and design of the study, interpretation of data, obtaining funding, critical revision of the article for important intellectual content, final approval of the article.

JT: The conception and design of the study, interpretation of data, obtaining funding, drafting the article, critical revision of the article for important intellectual content, final approval of the article.

**Ethics**

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

This study has the permission from the National Agency of Medicolegal Affairs, Helsinki, Finland; permission 1781/32/200/01.

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**Competing interests**

There were no conflicts of interest for any of the authors.

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